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Clinical Proceedings

OF THE CHILDREN'S HOSPITAL

WASHINGTON, D. C.

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PANEL SYMPOSIUM: MONILIASIS

MONILIASIS OF THE ORAL CAVITY

Leroy E. Hoeck, M.D.†

The occurrence of oral thrush, or moniliasis, or better still, infection with *Candida albicans* in a significant number of infants in the premature nursery at the District of Columbia General Hospital has recently given us the opportunity to study the disease in some detail. Oral thrush has been primarily only an annoyance because it responds quite promptly in most instances to local treatment. However, efforts to prevent its occurrence and attempts to uncover the cause have not met with complete success, so that the infection seldom has been wholly absent from the nurseries.

It is natural to think of a possible source of monilial infection as being the mother, because monilial vaginitis is quite common during pregnancy. This would allow new cases to be continuously introduced into the nursery with new admissions. However, in other studies, only a fraction of cases have been attributed to maternal sources. Nursery techniques and procedures, conduct of nursing and medical personnel in carrying out prescribed procedures, presence of monilial infections in personnel, the normal widespread presence of *C. albicans*, the varied forms of monilial infection and the possible predisposing effect of antibiotics are a few of the factors that can influence the incidence of infection. Help for the problem has come in the form of new and effective antifungal agents and from recently developed culture techniques which enable a more rapid and specific identification of *C. albicans*.

The common clinical picture of oral thrush presents as white, patchy, pearly lesions that are a little elevated and can be seen usually on the buccal mucosa, under the tongue, on the gums, under the lips, and often as a coated tongue. The pharynx seems to stay clear most of the time.

I should like to discuss some of the data that have been obtained from the study of 189 premature infants discharged from the nursery at D. C. General Hospital over a 16 month period from April 1956 through July 1957. An attempt was made to identify by laboratory means all suspected cases of thrush that were seen in the nursery during this time. Cultures were taken from the mouths and stools of infants at the onset of signs of thrush and were repeated in most instances on the fourth and seventh days thereafter.

* Transcript of a Metropolitan Area Pediatric Centers' Conference.

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From this experience we can say something about the course of the disease and something of the effectiveness of treatment. Gentian violet has long been a dependable, although somewhat messy, treatment. In this series of 189 cases, 75 babies were treated with gentian violet. When this substance is used as a ½ per cent solution applied locally to the lesions twice daily for five days it is usually effective, but in some cases which do not respond to that strength, the strength of the solution must be increased to 1 per cent; consequently, this latter percentage is the usual strength used. This schedule of treatment is an arbitrary one and clinical clearing is often noticed in two or three days. However if treatment is discontinued at two to three days many recurrences are noted.

Nystatin (Mycostatin®) has been receiving some attention for its effectiveness in the treatment of this disease, and 92 of the 189 cases were treated with this drug in various ways. There is evidence that just a trace of nystatin is absorbed into the blood stream from the intestine. Six babies were treated by gavage, with 50,000 units of nystatin in 10 ml. of distilled water given three times a day. Of these 6 cases, 4 cleared up in 6, 7, 8 and 10 days respectively. One infant after three days of treatment showed no improvement, and another had a bloody stool the day after medication was begun, so the drug was discontinued. This gives us evidence that there is some effect in clearing oral lesions even though the antibiotic is given without contact with the mouth. Six infants received 50,000 units of nystatin in the formula three times daily; this was ineffective and a change to another type of treatment was necessary.

In order to determine the normal course of thrush, seven babies were given no specific treatment but were kept under careful observation during the course of their disease. Of the seven, five required 9 to 17 days for the thrush to clear, one required six days and another just two days. Untreated thrush, therefore, is usually self-limited, but in general lasts a longer period of time than if treated.

In our series of cases, an effective method of treatment was that of giving a little water after every feeding, and then swabbing the mouth with the suspension of nystatin. This meant eight swabbings a day, but there was noticeable clearing in two to three days in most cases. The usual course of treatment was five days but on occasions this was extended for as long as 10 days.

It is hard to get any conclusive evidence in regard to the influence of antibiotics. Approximately 800 infants under 5 pounds birth weight were admitted to the nursery during this 16 month period. One hundred and sixty-seven of these, or 21 per cent, received an antibiotic of some sort. Of the 189 infants who developed thrush, 73, or 39 per cent, had received antibiotics. Since some of these babies were ill enough to require anti-

TABLE I

Age at onset	Incidence of thrush	Percentage
0–6 days	0	0
6–10 days	49	26
11–15 days	71	38
16–20 days	27	14
21–25 days	23	12
26–50 days	19	10

biotics, they may have been more susceptible to thrush. It is recalled also that thrush was a problem here long before broad spectrum antibiotics were available.

Another interesting factor was the time of appearance, or the age at onset of thrush. This is summarized in table I.

There is one other interesting sidelight. In a group of 110 premature babies of whom half were fed a simulated breast milk formula, and the remaining half a regular high protein-low fat formula, there were 19 cases of thrush. Five developed thrush while on the simulated breast milk formula and 14 developed it while on the high protein-low fat formula. This brings up other questions—whether there are secretions from the salivary glands that are having an effect and whether the serum calcium-phosphorus ratio and the parathyroid function play a part.

CUTANEOUS MONILIASIS

Alphonse P. Palmieri, M.D.*

Moniliasis as an entity has been known for over 100 years, but in recent years has stimulated renewed interest. There is an increasing number of articles dealing with moniliasis in association with antibiotic therapy, endocrinopathies, blood dyscrasias and other unusual syndromes.

The subject of cutaneous manifestations of moniliasis in infants and children will be briefly reviewed.

Causative Agent

The genus Candida, or Monilia, comprises yeastlike organisms of which five species are medically significant. Of these, *Candida albicans* is the most frequently encountered species in human disease. These organisms may be listed as intermediate between the dermatophytes and the deep mycoses.

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Incidence

Candida is a widespread organism. In normal children and adults, the incidence of positive oral and stool cultures was found to vary from 15 to 31 per cent. In this group the organism is considered as part of the normal intestinal flora but is rarely found as a normal inhabitant of the skin. In the newborn and young infant, the incidence of positive cultures varies from 1 to 37 per cent, but most investigators have shown that in this age group Candida is not part of the normal flora. Figures show that the actual incidence of the disease in infants ranges from 1 to 23 per cent. Most observers feel that the incidence of moniliasis is greater in the premature than in the full term infant. This may be influenced by a longer hospital stay, but one study showed that even during a comparable period of hospitalization the incidence of moniliasis is greater in the premature. It has also been found that bottle-fed babies have a higher incidence than breast-fed babies.

Epidemiology

Candida vaginitis in the mother is probably the commonest direct or indirect cause of thrush in the newborn. Infants born of these mothers have the disease earlier and more frequently than infants whose mothers have no monilial vaginitis. Other sources of infection are the hands of nurses and mothers with or without clinical disease. Nurses in intimate contact with infants who have thrush carry the organisms on their fingers for variable short periods of time. The disease can be contracted from contaminated nipples, diapers and other objects. Direct contact with contaminated saliva and airborne organism are other possible sources of infection. In children, Candida harbored as a saprophyte can be an endogenous source of disease. Exogenous infection is also possible.

Predisposing Factors

In general, cutaneous moniliasis does not occur with great ease unless there are predisposing factors. Briefly, the most important of these are maceration of the skin, diabetes, constitutional defects in the defense mechanism and possibly hypersensitivity. Other known predisposing factors are prolonged antibiotic therapy, debility and probably prematurity.

Skin Lesions

Because infants show a different clinical picture from children, the two age groups will be described separately. A recent well planned study in newborns has shown that 100 per cent of infants with positive oral smears

and cultures developed clinical moniliasis. This same study showed that infants with positive stool cultures had cutaneous moniliasis in 75 per cent of cases, and 98 per cent had combined cutaneous and oral moniliasis. This study indicates that young infants do not harbor Monilia normally and that in most cases of cutaneous moniliasis the source of infection is the stool.

In infants the skin disease is usually a rapidly spreading acute dermatitis. The lesions are superficial and start at the diaper area as tiny vesicles with surrounding erythema. These coalesce to form moist, shiny erythematous erosions with sharply defined raised scaling borders. Small satellite lesions of the same character may be present surrounding the original lesion. At times similar lesions may be found in other intertriginous areas, such as around the neck, in the axillae, behind the ears, and even on the face and scalp. More rarely the entire body may be affected. Variations in morphology may resemble seborrheic dermatitis, atopic dermatitis, ringworm and, when severe, Leiner's disease. Other rare manifestations in infants are vulvovaginitis, perlèche, balanitis, paronychia and onychia. In Negro infants there is usually depigmentation of the affected area. Because of its frequency moniliasis should be considered in the differential diagnosis of diaper rash, especially if the diaper lesions are resistant to conventional forms of treatment.

In contrast, in children moniliasis usually has a chronic and recurrent course, although acute cases have been described. As stated previously, the source of infection is usually endogenous. There may be a history of long-standing moniliasis dating back to infancy. The skin lesions in this age group are usually deeper than in infants. These lesions tend to be localized and more commonly start at the corners of the mouth. This process may spread to the scalp and cause alopecia. Other common locations are the eyelids, nose, elbows, knees, behind the ears, and on the nails and nailbeds. These lesions usually appear as weeping erythematous patches covered with crusts but they may also occur as dry erythematous plaques. There may be superficial vesicles filled with thin pus; these usually are present at the borders of the plaques. In some cases lesions resemble ringworm.

In rare instances, monilial granuloma, a deep inflammation of the skin, occurs. It usually begins as a simple thrush and ultimately involves the oral mucosa, face, finger nails and extremities. The condition is resistant to treatment and most reported cases have ended fatally.

Recently there have been reports in the literature of children with long-standing cutaneous moniliasis followed by hypoparathyroidism, or hypoadrenalism or both. In these cases the skin lesions precede the endocrinopathies by intervals of from 3 months to 13 years. The reason for

this relationship is at present not definitely known, but most observers feel that Monilia is superimposed on the dystrophic skin changes which precede the actual chemical change associated with the particular endocrine disturbance.

In both age groups id reactions may occur. The id reaction will occur only if there is a primary focus containing live fungi and if there is a high degree of skin sensitivity. These reactions may take on a variety of forms. The lesions are sterile and may be papular, urticarial, vesicular, bullous, purpuric or eczematous. They may be either localized or generalized.

A new antibiotic called nystatin (Mycostatin®) derived from streptomyces is up to this time the most promising therapeutic agent in moniliasis. It has been found by most observers that in cutaneous moniliasis the best results are obtained by combining topical therapy with oral administration of the drug.

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SYSTEMIC MONILIASIS

Marc L. West, M.D.*

Admittedly, cases of systemic moniliasis are rare but in most cases oral thrush was present at some time during the course of the illness. It is

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therefore quite possible that if the oral part of the disease had been eradicated the systemic complication might not have occurred. I shall cite some cases from the literature.

The first case is of Candida meningitis. The presence of Candida in the spinal fluid is somewhat rare and case histories in pediatric age groups are even more rare. Morris, Kalz, and Lotspeich report a case of monilial meningitis in a 23 year old adult.[1] The patient had had a dull, intermittent frontal headache for 10 months and a gradual loss of vision for three months prior to hospital admission. Finally, a right hemiplegia and vertigo appeared which led to hospitalization. A spinal tap at that time showed a pressure of 550 mm. and a cell count of 284 lymphocytes; the sugar and the protein were within normal limits. Because of the long history and the appearance of vertigo, a tentative diagnosis of a tumor of the third ventricle was made, even though it had been noted on admission that there was a white exudate on the tongue and the posterior pharynx. A ventriculogram showed an enlargement of both lateral ventricles and the third ventricle. Following this procedure, the patient's temperature rose to 104° F. This was interpreted as the onset of a bacterial meningitis. The patient was given sulfonamides for 30 days; the temperature returned to normal in one day. In addition, a course of radiation (2700r) was given to the base of the brain and the cervical portion of the cord, but the patient eventually died after eight weeks in the hospital. Prior to death, it had been noted that there were many round, doubly refractile bodies in the spinal fluid, a finding often interpreted as powder from a glove, but also consistent with the presence of a fungus infection. Candida was cultured from eight different spinal fluid specimens, and the oral lesions also turned out to be thrush. At autopsy, there was a thick, white exudate at the base of the brain and in the ventricles, at some points actually forming a granuloma and bridging from one side of the third ventricle to the other. This was a chronic process histologically, and in fact, was a fungus tumor.

The next entity is endocarditis due to *Candida albicans*. This is also exceedingly rare in the pediatric age group. Until 1952, only one case had been reported in a child (a 14 year old), and in that case there was some doubt as to the exact classification of the fungus. The first case of monilial endocarditis reported in an infant[2] occurred in a 7 month old white infant who had a history of cough for six months, and a fever for two weeks prior to admission. Because of the onset of fever, pertussis was suspected and the child was admitted to the hospital. An x-ray at that time showed a middle lobe pneumonia with some atelectasis. There were no cardiac findings at that time, and the liver and spleen were not enlarged. During the hospital stay there were repeated bouts of fever

for which the patient was given sulfadiazine and penicillin, resulting in only temporary improvement in the fever, and no change whatsoever in the pulmonary findings. After a month in the hospital, bronchoscopy was done. At this time, a severe oral thrush had appeared, and following the bronchoscopy the pulmonary lesions became bilateral and more severe. By the end of two months of hospitalization, a blood culture yielded *C. albicans*, and a few days later the patient died. At autopsy, yellowish nodules were found on the leaflets of the mitral valve and there was an abscess of the interventricular septum. Similar yellow nodules were seen in the liver. Candida was grown from all these lesions. The lungs were apparently not involved by the Candida, and a causative factor for the chronic pulmonary disease could not be found. The blood culture that yielded Candida was obtained only after the bronchoscopy and after about four weeks of antibiotic therapy, so it was thought that the trauma of bronchoscopy plus the prolonged antibiotic therapy resulted in the spread of infection and the endocarditis.

The British describe a pharyngeal incoordination with esophagitis due to Monilia. A typical case[3] is that of a 17 day old girl with a 24 hour history of vomiting and refusal of feedings. Thrush was seen in the mouth at this time. Therefore, treatment was started with 1 per cent gentian violet locally, and one teaspoonful of 0.01 per cent gentian violet three times a day orally. There was difficulty in swallowing; thick, profuse nasal and oral secretions appeared and recurrent periods of cyanosis followed episodes of apparent aspiration. Because of the patient's critical condition, hydroxystilbamidine was given intravenously in dosage of 5 mg. per Kg. every 12 hours. In addition she was given streptomycin, because of a possible aspiration pneumonitis. The baby slowly improved on this routine but she could not tolerate oral feedings for two or three weeks and required tube feeding. At fluoroscopic examination it was found that the normal swallowing mechanism was not operating and the lipiodol hung up in the pharynx, so that this material was aspirated into the nasopharynx and down into the trachea. The British feel that should an infant with oral thrush have feeding difficulties out of proportion to the lesions in the mouth, an esophageal lesion must be considered. They advise fluoroscopy with lipiodol to confirm the diagnosis. It is important to remember that after the oral lesions are cleared it still takes two or three weeks before the child is able to swallow.

Generalized fatal visceral involvement can occur.[4] This is exemplified by a 10 year old white boy with an 8 month history of cough, weight loss and anorexia. Prior to hospitalization, he had received 50,000 units of penicillin every two hours for two months and had continued to run a low grade fever during that time. In addition, he required multiple trans-

fusions because of a hypoplastic anemia. Finally, blood appeared in both his stool and sputum, and *Candida albicans* was recovered from the sputum. Roentgenogram of the chest showed a bilateral stringy type of soft tissue density radiating from the hilar regions. In the last four weeks of life a severe oral thrush appeared and was treated with iodide and gentian violet locally with no response. The patient was also given chloramphenicol for the last four weeks of life. At autopsy there were areas of thrush in the myocardium; there was a nodular, slimy appearance to the surface of the lungs; the thyroid in cut section exuded greenish pus; and the kidney was studded with greenish areas, which, when cut, also exuded pus. Material from all these areas grew *C. albicans* on culture. Staphylococcus was cultured from the lungs. In retrospect, the cough, fever and anorexia were probably due to monilial infection of the mouth which had spread to the bronchi. The long-term antibiotic therapy probably precipitated the final generalized spread of this lesion.

It is well known that the incidence of thrush with hypoparathyroidism is high enough so that it cannot be considered due to chance, but the etiological relationship is still obscure. In a series reported by Steinberg and Waldron in 1952,[5] there were 52 cases of hypoparathyroidism of which 7 had associated oral or cutaneous moniliasis. Three of these 7 cases also had symptoms of Addison's disease. At pathological examination, no monilia organisms were recovered from either the adrenal or parathyroid glands. It is known that following surgical hypoparathyroidism, there is no thrush. It is also known that in idiopathic hypoparathyroidism even when the patient's serum calcium concentration returns to normal, the thrush does not disappear. Again, in many of these cases, the thrush is present long before the clinical manifestations of hypoparathyroidism become apparent.

Acrodermatitis enteropathica is a disease entity which includes loss of hair, dwarfism, a prolonged episode of diarrhea and some unusual skin lesions. These skin lesions first appear around the mouth, in the perineum, and almost symmetrically on the distal parts of the arms and legs. Initially, they are vesicular and pustular and may be mistaken for impetigo. The chronic appearance is that of a red, scaly, erythematous lesion. Candida is often grown from the stool during these episodes of diarrhea.

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THE LABORATORY ASPECTS OF MONILIASIS

Joseph C. Stone*

Of all the fungi isolated from human sources, the group of yeastlike fungi has been the most difficult to study because of the great differences of opinion concerning criteria to be used in classification. For example, in the literature there are to be found 172 synonyms for the single species *Candida albicans*. More recently, better methods of classification have been developed and it has been possible to reduce the mycelium-producing, nonascospore-forming, yeastlike fungi to a single genus, Candida, which contains comparatively few valid species. *C. albicans* is the only member of this genus which is pathogenic for laboratory animals. The familiar generic name Monilia now has been replaced by the name Candida.

The discussion of the genus Candida has been a controversial issue among mycologists for a long time and the term Candida is being used until the Botanical Congress sees fit to change it. This genus includes 30 species with six varieties, *C. krusei*, *C. parakrusei*, *C. tropicalis*, *C. pseudotropicalis*, *C. stellatoidea*, and *C. guilliermondi*.

C. albicans may be isolated from skin, oral or vaginal mucous membranes and stools in at least 15 to 20 per cent of normal individuals. The organism has also been isolated from soils and decaying vegetation.

Source of Infected Material

Collection of infected material for examination varies considerably depending upon the type of clinical symptoms. Skin or nail scrapings,

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mucous patches from the mouth, vagina or anus, sputum, blood or cerebrospinal fluid, or feces may be collected for laboratory study in sterile containers or as smears on slides. Swabs are satisfactory if they are streaked on the media immediately or if they have been kept moist with sterile saline.

Examination of Infected Material

Skin and nail scrapings should be mounted in 10 per cent potassium hydroxide in the usual manner with a cover glass and heated gently. Sputum or mucous material should be pressed to a thin film with a cover glass on a slide. The latter materials may also be stained by Gram's method, but a diagnosis of *C. albicans* should not be made from this smear.

Microscopically, species of Candida appear on the stained slides or direct mounts as small, oval, thin-walled, budding cells about 2 to 6 microns in diameter. Since nonpathogenic yeasts may look similar to pathogenic yeasts, special methods of culturing are necessary for identification.

Infected material including scrapings, swabs, sputum, pus or other materials should be cultured on Sabouraud's glucose agar at room temperature and at 37°C. The addition of penicillin and streptomycin, or chloramphenicol and actidione, if desired, will prevent contamination in the cultures. Many nonpathogenic yeasts will not tolerate actidione. A number of other media may be used for isolation of the yeasts.

Cream-colored, smooth, pasty colonies of *C. albicans* appear on Sabouraud's glucose agar in three or four days and have a yeasty odor.

Newer Culture Methods

The identification of this pathogen from clinical specimens as it is attempted by most laboratory personnel requires time-consuming and complicated procedures. Growth on conventional Sabouraud's or other mycological media in 24 to 72 hours may provide a means of presumptively identifying a yeast or yeastlike organism. Research workers and technicians have been trying to devise better methods and procedures for the more rapid identification of *C. albicans* by means of inducing the characteristic chlamydospores; this is the only definite criterion *in vitro* for the differentiation of this pathogen.

Reid, Jones and Carter,[1] devised a polysaccharide-free medium containing zein, the basic protein of corn meal, for the demonstration of chlamydospores of *C. albicans*; their results were fair after 24 hours incubation.

Nickerson and Mankowski[2] devised a synthetic medium containing a polysaccharide that encourages chlamydospore production as the carbon source, but other authors have questioned this as an over-all advantage.

Fusillo, Learnard and Dozier,[3] utilized difco-dehydrated chicken plasma placed on a slide and incubated at 30° C.; this provided a transparent view of the chlamydospore formation. This procedure is too time-consuming and costly even though results were achieved in 18 hours. Other workers in this field have stated that with this method it was difficult to distinguish between germinal tubes and pseudomyceliums.

Vogul and Moses,[4] introduced the Weld method for identification of *C. albicans* by use of the EMB agar plate. This produced spidery colonies within 24 to 48 hours when incubated at 37° C. in an atmosphere containing 10 per cent carbon dioxide. Other species in the genus Candida produce this same type of colonies on this and other media.

Liu and Newton[5] used a buffered alkaline medium without nutrients to produce the chlamydospores.

Pigmentation Methods: The Pagano-Levin culture medium, which is designated to isolate yeasts and at the same time differentiate *C. albicans* from nonpathogenic yeasts, requires three days of growth at room temperature, and the variation of the pigmentation may be confusing. However, it had, in our experience, an advantage over the Nickerson medium used for the same purpose, in that the latter only separates the genera of Candida.

Stein,[6] compared a rice medium by Taschdjian with the polysaccharide medium by Nickerson and Mankowski and claimed greater chlamydospore formation with rice medium. Subsequently, Taschdjian[7] described a cream of rice infusion with Tween 80 agar which produces the characteristic chlamydospore formations in as little as 14 hours. The medium is easily prepared and the organisms are examined with the high power objective using no. 15 oculars; the plate can be poured thin, thus conserving agar. It does not easily support growth of bacteria or contaminant fungi and can be swabbed or streaked with a loop or sterile applicator stick *directly* from the clinical materials. The chlamydospore formation is observed in less than 24 hours, and before macroscopic growth of the yeastlike colonies can be seen on other routine media. We are using this medium with the other media as controls, and it is proving to be a superior method of identification of *C. albicans* from most clinical materials.

Chlamydospore formation is the only real criterion in the laboratory diagnosis of *C. albicans*, and rice infusion medium with Tween 80 is the most rapid and reliable culture method up to the present time. When *C. albicans* is suspected of being the sole etiologic agent causing death, fermentation, pathological, immunological, and animal studies should be conducted.

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SWELLINGS OF THE PAROTID GLAND

John Tkacz, M.D.*

The pediatrician of a patient with parotid gland swelling—especially if tumor were suspected—would think the information in most texts inadequate. Therefore, the various etiologies of parotid gland swelling in the pediatric age group will be discussed, with the emphasis on parotid tumors, especially those occurring in children under 1 year of age.

CASE REPORT

J.W., a 13 year old white girl, was admitted to Children's Hospital on August 12, 1957 because of a mass in her right retromandibular area. Five months prior to admission the mass was first noted; the family physician diagnosed it then as mumps. Six weeks prior to admission the patient had been brought to the Out Patient Department because of increasing size of the mass. She had had some pain in the area for one day a few months previously, but during the rest of the time she had experienced no

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discomfort. The mass had not undergone any apparent change. It was firm, smooth, 2 by 2 by ½ inches in size, nontender, freely movable and was located posterior and lateral to the angle of the right mandible. The skin overlying the mass was of normal color and temperature. There was no remarkable adenopathy in the neck.

The patient was presented to the Tumor Board whose impressions were that the tumor was probably parotid gland swelling and that one possible cause of the swelling might be a stone in the salivary duct. On July 7, 1957 the duct was probed but no stone was found. On July 11 a sialogram was done by the ENT service using Pantopaque® as the contrast medium. It revealed normal arborization indicating that the tumor was probably noninfiltrative; the ductal system appeared slightly displaced anterolaterally by the tumor. The patient was again seen by the Tumor Board on July 31. Its impression then was either a branchial cleft cyst or parotid tumor; its recommendation was surgical excision.

On August 12 the patient was admitted for surgery. Past history revealed that she "had mumps twice"; the "mumps" occurred three years and two years prior to admission, once bilaterally and once unilaterally. On admission the patient was well developed, well nourished, alert and in no distress.

On August 13 surgery was performed. An encapsulated tumor of the right parotid gland was found. Frozen section was done and was reported as benign mixed tumor of the parotid gland. Excision of the tumor was performed with considerable care to avoid damage to the facial nerve. Postoperative course was uneventful: no paralysis ensued; a minimal paresis of the right angle of the mouth was noted, but thought to be only temporary. Pathological diagnosis was benign mixed tumor of the parotid gland.

DISCUSSION

The two parotid glands drain into the mouth through Stensen's duct opposite the upper second molar on the inside of each cheek. The parotid glands normally secrete a clear serous fluid that does not contain mucin. Frequent infection by way of the duct is undoubtedly prevented by the steady flow of saliva. The absence of mucin, which is somewhat antibacterial, does seem to make the parotids more subject to infection than the submaxillary and sublingual glands, each of which secretes both mucinous and serous fluid. Enlargement of the salivary glands is more commonly due to infection than to any other cause. Swelling of the parotid gland may be encountered in the following conditions:

(1) Parotitis due to the specific viral infection of mumps with or without submaxillary, sublingual and submental gland involvement.

(2) Parotitis due to bacterial infection:
   (a) recurrent parotitis
   (b) suppurative parotitis.

(3) Infiltration of the glands by tumors such as lymphosarcoma, by leukemic cells, or by the specific lesions of tuberculosis, sarcoidosis, syphilis, and typhoid fever.

(4) Miscellaneous conditions such as enlargement of lymphatics in or adjacent to the glands, calculi or food particles obstructing Stensen's

duct, allergy, iodide or mercurial medication, or operative trauma. Emphysematous parotitis has been noted in children who had been blowing on rubber balloons or toy instruments.

(5) Parotid gland tumors.

When parotid gland swelling is present, the ramus of the jaw normally cannot be felt. The absence of swelling or redness of the salivary gland duct opening is of no diagnostic significance. In all cases of parotid gland swelling the duct should be milked. In mumps there is either no secretion or a clear one, but never a cloudy or purulent one. A cloudy or purulent secretion means either recurrent or suppurative parotitis. If there is a frank or impending abscess of the gland, suppurative parotitis is present; if no abscess is found, recurrent parotitis is present. Suppurative parotitis usually necessitates incision and drainage; it occurs most commonly in the newborn and in the aged but may occur in children. Recurrent parotitis is a condition that occurs in otherwise healthy children. Operative trauma occasionally produces a suppurative parotitis.

Calculi in the salivary glands or ducts occur in adults but are extremely rare in children. In Mickulicz's syndrome there is swelling of the parotids usually due to leukemic infiltration of the gland, lymphosarcoma, tuberculosis or syphilis. Sarcoidosis may involve the parotid glands. Overdoses of, or sensitivity to, iodides, mercurials and lead can cause parotid swelling. There is some evidence that allergy may cause parotid swelling; a few cases have been reported in children. Parotitis may occur in typhoid fever. In cat scratch fever with a lesion of the conjunctiva or the face there may be nodular swellings in the parotid area due to lymphadenitis. Tuberculosis may also involve these lymph nodes. Cervical adenitis and cellulitis may cause confusion but in these conditions the ramus of the jaw usually is normally palpable.

TRUE PAROTID GLAND TUMORS

The first symptom in most cases of salivary gland tumor is a painless unilateral swelling. Pain is rarely a symptom of benign tumors but invariably occurs in the later stages of cancer. Even the malignant tumors are usually noninvasive so that the adjacent structures are displaced rather than infiltrated by the tumor. In the parotid area the tumor usually grows outward except in the portion of the gland which hooks around the ascending ramus of the mandible. Tumors arising in this area cannot expand externally because of the bony structure, and consequently may bulge into the lateral pharyngeal wall in the tonsillar region. In most instances the tumors are located at the angle of the jaw, and are usually directly in front of, but occasionally posterior to, the ear lobe. However, parotid tumors may also occur along the zygoma or in any region along a line

extending from the zygoma in a semicircular manner to the angle of the jaw and posterior to the mastoid process; they may, in addition, occur in the pharynx. The smaller tumors are usually smooth but those larger than 5 cm. in size are often nodular. Most of the tumors are slow growing; it usually takes one year or more before the average tumor reaches a size of 2 cm. There may be a delay of months before medical attention is sought; one study of adults with parotid tumors revealed an average delay of 42 months!

In 1950, Howard, et al., reported 21 cases of tumorous enlargements of parotid glands developing in childhood, and, in addition, reviewed the literature. Their series of cases and the cases which they collected from the literature, a total of 190, included only those in which the parotid tumors were noted in patients younger than 16 years of age. The types of tumefactions of the parotid salivary gland encountered in their material and literature survey were listed as follows:

I. Inflammatory lesions. Chronic recurring infection of the parotid gland and its duct may produce a fibrotic nodular gland which may simulate a tumor and make a clinical differentiation impossible. This disease has its onset in childhood. Exacerbations of acute swelling of the gland occur and frequently are bilateral. If with such a history a patient develops a nodule in the parotid, chronic parotitis should be considered. Four cases were reported.

II. Neoplasms of connective tissue arising only incidentally in the parotid gland:

1. *Vascular tumors* are the characteristic tumor of the parotid gland in the first year of life, occasional examples having been noted at birth. The hemangioendothelioma of infancy usually runs a benign course. Fifty-three cases of hemangioma and 6 of hemangioendothelioma were reported.

2. *Lipomas* are an uncommon finding within the parotid gland. Four cases were reported.

3. *Sarcomas* rarely occur in the salivary gland. Many pathologists doubted the accuracy of diagnosis in the reported cases, believing many of them to be undifferentiated carcinoma or hemangioendothelioma. Ten cases were reported.

III. Neoplasms of the salivary gland *per se*:

1. *The mixed tumor* should be considered a nonmetastasizing neoplasm. Local invasion is seen only rarely. The local recurrences often noted following excision of these tumors are probably explained by a multicentric origin of the lesion. Seventy-two cases were reported.

2. *The papillary cystadenoma lymphomatosum* is an encapsulated, usually small tumor which contains many small cysts. The origin of the tumor is uncertain but most authors attribute the lesion to an embryonal mal-

formation. The tumor characteristically appears in old age. Four cases were reported.

3. *The carcinoma* is a malignant epithelial tumor by definition. In adults this tumor is highly malignant. Twenty-six cases of parotid carcinoma (which included cylindroma) were reported.

From this group of parotid carcinomas two entities have been separated which are clinically as well as histologically distinct from the general group of carcinomas, namely, the cylindroma and the mucoepidermoid tumor.

4. *The cylindroma* is a malignant tumor with a slow course, often lasting 20 years or more. It is locally invasive and metastasizes frequently, but late, to the regional lymph nodes and to the lungs. Cases of cylindroma were not reported separately but were included in the reported cases of parotid carcinoma.

5. *The mucoepidermoid tumor* is a malignant epithelial neoplasm which has epidermoid features and at the same time secretes mucin. There are two groups, one a low grade malignancy, the other of higher malignancy. Seven cases were reported.

IV. Miscellaneous, including parotid cysts:

1. *Parotid cysts:* One case was reported.

2. *Secondary neuroblastomas* have invaded the lower pole of the parotid gland by extension from an involved cervical sympathetic chain. Two cases were reported.

3. *Accessory lobe of the parotid simulating a parotid tumor:* One case was reported.

The incidence of primary parotid neoplasm calculated from these above cases in the report by Howard, et al., (which is based on a total of 190 patients younger than 16 years of age) is as follows:

Mixed tumors	39%
Hemangiomas	29%
Carcinomas	18%
Sarcomas	5%
Hemangioendotheliomas	3%
Lipomas	2%
Papillary cystadenomas lymphomatosum	2%

PAROTID TUMORS IN THE FIRST YEAR OF LIFE

Vascular tumors are the characteristic tumors of the parotid gland in the first year of life. Campbell in 1956 reported three vascular tumors of the parotid gland, making a total of 62 reported cases (Howard, et al., had already mentioned 59 cases in their report and literature review). Both capillary and cavernous hemangiomas of the parotid gland may be merely slightly differing manifestations of the congenital vascular dysplasias of

the head and neck region that are familiar in the form of cutaneous port-wine strains. In fact, hemangiomas of the overlying skin are common associated lesions.

Of the 62 cases noted above, 36 of the 51 patients whose sex was recorded were girls. The right and left parotid glands appear to have been involved with approximately equal frequency. McFarland recorded only 3 cases in which another major salivary gland, the submandibular, was affected. Strikingly, he found that 90 per cent of parotid tumors recorded in infants in their first year were hemangiomas. Eighty-eight per cent of all recorded hemangiomas of the parotid gland affected infants in this age group.

The value of present statistics is diminished by the probably large number of unreported cases. In the files of one pediatric hospital, reference was found to 14 unpublished cases of hemangioma of the parotid gland. Nevertheless, the available statistics indicate that chronic unilateral enlargement of the parotid gland in the first year of life is usually a symptom of parotid hemangioma. Obvious hemangiomatous involvement or bluish discoloration of the overlying skin and the compressibility of some of the lesions lend support to a preliminary diagnosis of parotid hemangioma. Biopsy is necessary, however, to exclude mixed tumor and carcinoma, both of which have been found to occur in the parotid gland in this age group. Table I presents the incidence of these three tumors occurring in the first year of life. In any event, surgical extirpation of the entire affected gland, subtotal parotidectomy with excision of the lesion, or biopsy followed by x-ray therapy have been favored as satisfactory definitive treatment for parotid hemangiomas.

TABLE I

Types of Parotid Neoplasms Occurring in the First Year of Life (after Campbell)

Neoplasm	Number of Cases	Percentage Occurrence
Hemangiomas	54	90
Mixed tumors	5	8
Carcinomas	1	2

TABLE II

Age Distribution of Patients with Hemangiomas of the Parotid Gland (after Campbell)

Age Years	Number of Cases	Percentage
0–1	54	88
1–12	6	10
Adults	1	2

Table II presents the occurrence of parotid hemangiomas at all ages as collected by Campbell. Forty-six of these 60 cases of the parotid hemangiomas in children up to 12 years of age were treated primarily by excisional surgery. Twenty-eight of these operations appear to have led to uncomplicated ablation of the tumor. Nine patients suffered from facial palsy. There were five postoperative recurrences and two deaths. All postoperative recurrences yielded to re-excision, but in 2 cases re-excision led to facial palsy. The extent of the operation is often not specified. Five of these patients were followed for periods of 10 years or more, and 4 for periods of one to five years, during which no recurrences were detected.

The chief danger inherent in parotid hemangiomas appears to be permanent damage to the facial nerve during surgical removal. As Howard, and Wawro and associates have pointed out, the facial nerve is encountered in the parotid region of infants at a deceptively superficial level and is therefore susceptible to unintended trauma. In the light of what is known of the behavior of congenital capillary hemangiomas of the parotid gland, the planned resection of portions of the facial nerve as part of primary excision for this lesion could be described as an unwarranted procedure, despite the excuses that have been made for it.

Despite a note of alarm sounded by Glaser, Mehn and Schultz, respecting a "uniformly disastrous course" that is "changed considerably" if surgical intervention occurs, there are but two references to parotid hemangiomas, the courses of which, not interrupted surgically, have terminated in death. An equal number of deaths have followed surgery. Wawro and his associates could find no reference to malignant variants of this lesion.

As with any tumor in childhood, one should consider all parotid tumors to be malignant unless proved otherwise. Cystic masses which were once considered benign must also be considered malignant. Small discrete masses which do not involve the facial nerve should be excised *in toto* for histologic diagnosis. With the larger lesions, however, because of the danger of facial nerve damage and in view of the chance of finding chronic parotitis indistinguishable from neoplasm by clinical means, incisional biopsy is preferable. Potential benefits of postoperative x-ray therapy must be weighed against the possibility of irradiation damage to the neighboring bone and eye.

SUMMARY

Parotid gland swelling is most commonly due to infection. Causes of parotid gland swelling include mumps, bacterial infection, leukemic infiltration, lymphosarcoma, tuberculosis, syphilis, calculi, tumors, allergy, sarcoidosis, mercurial medication, iodide medication, and operative trauma.

Vascular tumors are the characteristic tumor of the first year of life; however, mixed tumors and carcinomas of the parotid gland have been reported in this age group.

Incidence of the types of parotid tumors based on Howard's figures on patients younger than 16 years of age (total of 190 cases) is: mixed tumors, 39 per cent; hemangiomas, 29 per cent; carcinomas, 18 per cent; sarcomas, 5 per cent; hemangioendotheliomas, 3 per cent; lipomas, 2 per cent; and papillary cystadenomas lymphomatosum, 2 per cent.

When parotid tumor is suspected, surgery is indicated at least to establish the proper diagnosis. Permanent damage to the facial nerve is the chief danger inherent in excision of the parotid tumor.

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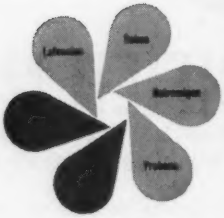

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